-binding proteins; The S-100 protein family; Novel members of the EF-hand calcium-binding protein family in normal and transformed cells; Calcium-binding proteins in bacteria, fungi and invertebrates; Structure, function and evolution; Calcium fluxes, binding and metabolism; Calcium-dependent and phospholipid-binding proteins in health and disease.

In the first section the members of the EF-hand homolog family are identified and characterized and thereby distinguished from several similar analogs. Undoubtedly future research will reveal additional EF-hand homolog subfamilies and functions in relation to Ca^{2+}-signaling. This section also includes a survey of the Ca^{2+}-binding proteins of the EF-hand type, the annexin family and also describes a dye that can be used to probe the conformational features of Ca^{2+}-binding proteins.

In section two, the S-100 protein family is discussed in detail, starting with an instructive biochemical and functional overview by Hilt and Kligman. Interestingly, the S-100 proteins are a group of small acidic Ca^{2+}-binding proteins that are expressed specifically in various types of cells and hence may be involved in transducing the Ca^{2+} signal in a cell-type dependent fashion. They may exert their effects by regulating the phosphorylation of specific effector proteins involved in signal-transduction, cell motility and cytokinesis, cellular differentiation, cell-cycle progression and inflammation. This section also lists in a Table the members of the S-100 protein family and proteins which have been shown to be synonyms or species homologs of any of the family members. Each of these proteins is briefly discussed. For example, MRP8 and MRP14 are two Ca^{2+}-binding proteins expressed during myelopoiesis. Interestingly, MRP14 plasma levels are elevated in cystic fibrosis and a variety of other pathological conditions. MRP8 is mainly expressed in chronic inflammation like rheumatoid arthritis.

In section three, novel Ca^{2+}-binding proteins of the EF-hand protein family are discussed in relation to normal and transformed cells. Non-muscle α-actinin is an EF-hand Ca^{2+}-binding protein, likely to assist the sarcomeric unit to withstand the force generated by the actin–myosin contraction. This protein may anchor actin filaments to the plasma membrane of non-muscle cells. α-Actinin contains two EF-hand structures close to the carboxyl-terminals and is involved in the reorganization of the cytoskeleton, which is of importance for cellular processes such as motility, cytokinesis, phagocytosis and secretion. It is of interest that β-crystallin, which is a Ca^{2+}-binding protein of the eye lens, loses its ability to bind Ca^{2+} with age, a phenomenon likely to take place also in cataract.

Section four gives a detailed account for the Ca^{2+}-binding proteins in bacteria, fungi and invertebrates. Of special interest is the Ca^{2+}-binding site of the D-galactose/D-glucose-binding protein of Gram-negative bacteria as well as the discussion about a novel Ca^{2+}-binding protein encoded in the shaker locus of *Drosophila*.

In section five, the Ca^{2+}-binding sites of various ion-channels are discussed. It is evident that four Na^+ channel α1 polypeptides and one dihydropyridine-sensitive Ca^{2+}-channel α1 polypeptide have putative EF-hand type Ca^{2+}-binding sites near their carboxyl-terminals. It is suggested that voltage-gated Na^+-channels and Ca^{2+}-channels, but not K^+-channels, can bind Ca^{2+} with portions of their internal sequences. In an interesting chapter by Erne *et al.*, alterations in cellular Ca^{2+} handling is discussed in relation to hypertension and human cardiac hyperthrophy. It is suggested that abnormalities of Ca^{2+} metabolism are involved in the pathogenesis of established human hypertension. Direct comparison of Ca^{2+} channels in vascular cells, from a neonatal spontaneous hypertensive versus normotensive rat strain, showed an enhanced probability for an opening and larger Ca^{2+} currents of the sustained type in genetic hypertension. In addition, the free cytoplasmic Ca^{2+} concentration is elevated at rest in localized regions of vascular muscle cells from spontaneously hypertensive rats. These findings were confirmed by confocal laser scan microscopy, indicating a subsarcolemmal increase in cytoplasmic free Ca^{2+} in the vascular muscle cell.

Section six deals with the Ca^{2+}-dependent and phospholipid-binding proteins in health and disease. This section is devoted to the diversity in the annexin family, annexin 1 and its biochemical properties and as well to a more clinical oriented chapter concerning the anti-inflammatory activity of human recombinant lipocortin 1.

Despite the fact that this book does not present a number of novel data and new concepts, it is of interest to all those who are engaged in the field of Ca^{2+}-signaling research. The rapid progress made in terms of identification of novel Ca^{2+}-binding proteins is not always parallelled by assigning them a function and consequently future research is needed to establish a role for the various Ca^{2+}-binding proteins not only in physiology but maybe more interestingly in pathophysiology.

Per-Olof Berggren

DNA Topoisomerases in Cancer; Edited by M. Potmesil and K.W. Kohn; Oxford University Press Oxford; New York, 1991; xv + 331 pages. £65.00

This informative book contains updated contributions from work presented at international conferences on DNA topoisomerases in cancer chemotherapy held in 1986 and 1988 in New York City in association with the New York University Post-Graduate Medical School and the Rita and Stanley H. Kaplan Cancer Center. DNA topoisomerases are important cellular enzymes involved in many aspects of DNA function such as DNA replication. These enzymes change the superhelical structure of DNA and are classified as type I and type II according to their mechanism of action. Type I DNA topoisomerases introduce transient single-strand DNA breaks, while type II DNA topoisomerases break both DNA strands to enable another duplex DNA segment to pass through. The relaxation of DNA supercoils is one of the major catalytic functions of topoisomerases, although bacterial DNA topoisomerase II (bacterial DNA gyrase) introduces negative supercoils. Inhibitors of bacterial DNA gyrase such as nalidixic acid have been used therapeutically in the treatment of bacterial infections. DNA topoisomerases have been found to be a successful target site for the chemotherapy of certain cancers. The interaction between DNA topoisomerases and chemotherapeutic agents developed for this purpose is examined in this book.

This book is organized into five main sections, which follow a good comprehensive introductory chapter. The first section (chapters 2–7) covers the basic aspects of the genetics and biochemistry of prokaryotic and eukaryotic DNA topoisomerases I and II. This section includes an examination in chapter 6 of inhibitors of bacterial DNA gyrase such as the etoposide VP-16, which may offer a new approach to antitrypanosomal chemotherapy. The use of yeast permeability mutants as a genetic system that facilitates the study of antitumour drugs such as camptothecin, etoposides and teniposides targeted at DNA topoisomerases is discussed in chapter 7. Purified yeast DNA topoisomerases I and II are similar to their mammalian counterparts in their interaction with these antitumour agents.

The second section of this book (chapters 8–15) examines inhibitors of topoisomerase I, including the natural product campothecin. This ia followed by a third section on inhibitors of topoisomerase II (chapters 16–19) The modification of the effects of topoisomerase inhibitors by the presence of other DNA binders such as polyamines is alo considered. The clinical problem of the resistance of cancer cell topoisomerases to the drugs against them is the theme of the fourth section (chapters 20–22). Multidrug resistance (MDR) is a particularly serious problem in many types of cancer or leukaemia and is associated with the overproduction of the integral membrane P-glycoprotein. The resistance associated with DNA topoisomerases, however, appears to be related to altered requirements of the topoisomerase enzymes and is denoted as atMDR where 'at' is altered topoisomerase (chapter 21). Finally, the fifth section (chapters 23–25) deals with the development and clinical use of topoisomerase inhibitors. These are used in the chemotherapy of patients with locally advanced or metastatic colon cancer. It has been found that two derivatives of camptothecin, 9-amino-20(RS) and 10,11-methylene-dioxy-20(RS) give long-term disease-free remissions and are of low toxicity (chapter 24). They also appear to by-pass the problem of cellular resistance mechanism in cancer cells.

This comprehensive volume deals in depth with a wide range of topics relating to DNA topoisomerase with particular emphasis on the relationship to cancer chemotherapy. The individual chapters are well documented and there is an adequate index. This book will be of great use as a source of both background reading and detailed material on this important subject area where cell biology and enzymology advance cancer therapies.

Helen Wiseman

New Drugs for Asthma Therapy (Agents and Actions supplements, vol 34); Edited by G.P. Anderson, I.D. Chapman and J. Morley; Birckhauser-Verlag; Basel/Boston/Berlin, 1991; x + 548 pages, Sw.Fr.148.00

This book constitutes the proceedings of an IUPHAR satellite symposium entitled 'New Drugs for Asthma' organised by the editors, Anderson, Chapman and Morley, in 1990. The title is somewhat misleading since the majority of papers discuss the pharmacology of compounds under early investigation by various pharmaceutical companies. Furthermore, approximately 25% of the papers do not discuss any therapy for asthma, potential or otherwise, but focus on the use of animal preparations, usually guinea-pigs, to evaluate novel therapies.

The book is divided into four sections, the first being devoted to bronchodilator drugs. Three papers review recent advances in the area of β_2-adrenoceptor agonists, which have led to the development of two long-acting compounds, salmeterol and formoterol, and the terbutaline pro-drug, bambuterol. These agents clearly provide the standard against which any novel bronchodilator agent will have to be assessed. Furthermore, evidence suggests that the new, long-acting β_2-adrenoceptor agonist, salmeterol, may possess clinically useful anti-inflammatory actions, which the short-acting compounds do no. Against this background, the other papers in the section address the therapeutic potential of selective phosphodiesterase inhibitors, muscarinic agonists and potassium channel opening agents. Unfortunately, few of these agents have been extensively evaluated in man, and their true therapeutic potential remains unclear.

The next two sections of this book are devoted to 'Inhibitors of Allergic Mediators as Targets' and 'Prophylactic Anti-Asthmatic Drugs', respectively. They contain a series of papers which describe different approaches aimed at either preventing the generation and release of pharmacological mediators, or blocking the action of specific mediators. One highlight in this section is data from clinical studies with the thromboxane receptor antagonist, GR32191. It appears to demonstrate that thromboxane receptor activation is not important in asthmatic bronchoconstriction. The rest of the papers in this section describe the clinical and animal pharmacology of leukotriene receptor antagonists and inhibitors of leukotriene synthesis, and the evaluation of a number of PAF receptor antagonists, antihistamines and a range of agents of undefined mechanism, which modify various aspects of allergic reactions in sensitised animals.

Notable omissions from these sections are papers on the pharmacology of tachykinin antagonists, an equally valid approach to a specific inhibitor of a putative allergic mediator, and an overview of the pharmacology of glucocorticoids, agents which currently account for the majority of prophylactic therapy in asthma.

The remainder of the book, in a section entitled 'New approaches to Anti-Asthma Drug Detection', is a collection of papers outlining methods of evaluating prospective therapies in animal preparations. The highlight of this section is a paper describing studies on the expression of the leukocyte adhesion molecules ICAM-1 and ELAM-1 during the response of sensitised primates to allergen, and the effect of antisera to these molecules on inflammatory cell recruitment and bronchial hyperreactivity. In this paper the case is made for an inhibitor of ICAM-1 as a therapy for asthma.

In conclusion, this book may be of interest to those engaged in or entering the area of asthma research. However, the price seems rather high for a book which is already two years old. Therefore, I suspect more copies will be found in libraries than in personal collections.

C.J. Whelan